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Tamara Alcaraz

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Jerry PELLETIER and Manjula DAS

Application No.: 09/807,047

Filing Date: April 6, 2001

For: OLIGONUCLEOTIDE PRIMERS THAT DESTABILIZE NON-SPECIFIC DUPLEX FORMATION AND USES THEREOF

Examiner: To Be Assigned

Group Art Unit: To Be Assigned

SUPPLEMENTAL PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of the above-captioned application, please enter the following amendments and remarks.

AMENDMENTS

In the Claims:

Please replace the complete set of claims by the new set submitted herewith.

1. A method for destabilizing non-specific duplex formation between a homopolymeric sequence of an oligonucleotide and a non-homopolymeric target nucleic acid, comprising a modification of said homopolymeric sequence of said oligonuclotide, wherein said modification decreases or abrogates hydrogen bonding between said modified homopolymeric sequence of said oligonucleotide and a non-homopolymeric target sequence.

2. The method of claim 1, wherein said modification is at least one universal base incorporated into said homopolymeric sequence.

3. The method of claim 2, wherein said universal base is 3-nitropyrrole.

4. The method of claim 1, wherein said oligonucleotide is a homopolymer comprising at least one nucleotide modification.

5. A method for increasing the proportion of full length cDNA clones in a library, comprising a use of a modified oligo d(T) homopolymer during first strand synthesis, wherein said modified oligo d(T) homopolymer comprises a modification which decreases or abrogates hydrogen bonding between said modified oligo d(T) homopolymer and a non-homopolymeric target sequence, thereby increasing the proportion of full length cDNA clones.

6. The method of claim 5, wherein said modification is at least one universal base incorporated into said oligo d(T) homopolymer.

7. The method of claim 6, wherein said universal base is 3-nitropyrrole.

8. The method of claim 5, wherein said modification is at least one chemically modified nucleoside incorporated into said oligo d(T) homopolymer.

9. The method of claim 5, wherein said modification is at least one base analog incorporated into said oligo d(T) homopolymer.

10. The method of claim 9, wherein said base analog is inosine.

11. The method of claim 5, wherein said modification is at least one mismatch incorporated into said oligo d(T) homopolymer.

12. The method of claim 5, wherein said modification is a phosphate or ribose modification incorporated into said oligo d(T) homopolymer.

13. The method according to claim 5, wherein an enzyme capable of RNA-dependent DNA polymerization is used for said first strand synthesis.

14. The method according to claim 13, wherein said enzyme is a reverse transcriptase selected from the group consisting of avian myoblastoid virus reverse transcriptase, murine moloney leukemia virus reverse transcriptase, and human immuno deficiency virus reverse transcriptase.

15. A kit for the synthesis of cDNA, said kit comprising a modified oligo d(T) homopolymeric primer, wherein said modified oligonucleotide includes a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence.

16. A method for reducing mispriming events during DNA synthesis comprising a use of a modified oligonucleotide to prime said DNA synthesis, wherein said modified oligonucleotide comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence, thereby reducing mispriming events, while maintaining a formation of a duplex with a homopolymeric target sequence.

17. The method of claim 16, wherein said modification is at least one universal base incorporated into said homopolymeric sequence.

18. The method of claim 17, wherein said universal base is 3-nitropyrrole.

19. The method of claim 16, wherein said oligonucleotide is a homopolymer.

20. A method for reducing mispriming during 5' RACE comprising a use of a modified oligonucleotide to prime said 5' RACE, wherein said modified oligonucleotide comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence, thereby reducing mispriming events while maintaining a formation of a duplex with a homopolymeric target sequence.

21. The method of claim 20, wherein said modification is at least one universal base incorporated into said homopolymeric sequence.

22. The method of claim 20, wherein said universal base is 3-nitropyrrole.

23. The method of claim 22, wherein said modification is at least one chemically modified nucleoside incorporated into said homopolymeric sequence.

24. The method of claim 20, wherein said modification is at least one base analog incorporated into said homopolymeric sequence.

25. The method of claim 24, wherein said base analog is inosine.

26. The method of claim 20, wherein said modification is at least one mismatch incorporated into said homopolymeric sequence.

27. The method of claim 20, wherein said modification is a phosphate or ribose modification incorporated into said homopolymeric sequence.

28. A kit for 5' RACE comprising a modified oligonucleoticle primer, comprising a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence.

29. A method for reducing mispriming during 3' RACE comprising a priming of said 3' RACE with a modified oligonucleotide, wherein said modified oligonucleoticle comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence, thereby reducing mispriming events while maintaining a formation of a duplex with a homopolymeric target sequence.

30. The method of claim 29, wherein said modification is at least one universal base incorporated into said homopolymeric sequence.

31. A method for generating *bona fide* genetic markers comprising a use of a modified oligonucleoticle to prime from homopolymeric stretch, wherein said modified oligonucleoticle comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence.

32. The method of claim 31, wherein said modified oligonucleotide primes from an internal A-rich region in an Alu repeat.

33. A method for stabilizing duplex formation between an oligonucleotide comprising a homopolymeric sequence and a target homopolymeric sequence comprising a modification of said homopolymeric sequence of said oligonucleotide, wherein said modification decreases or abrogates hydrogen bonding between same and non-homopolymeric target sequence, thereby stabilizing duplex formation between said oligonucleotide and said target sequence.

34. A method for reducing mispriming during sequencing comprising a use of a modified oligonucleotide to prime DNA synthesis, wherein said modified oligonucleotide comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence.

35. A method to improve the discrimination between a binding of an oligonucleotide homopolymeric sequence to its targeted homopolymeric sequence versus a non-homopolymeric sequence comprising an insertion into a homopolymeric sequence of said oligonucleotide of at least one modification which decreases or abrogates hydrogen bonding between same and said non-homopolymeric sequence.

36. A method for increasing the proportion of full length cDNA clones in a library, comprising a use of a modified oligonucleotide during second strand synthesis from a 3' end-tailed first strand product, wherein said modified oligonucleotide comprises a homopolymeric sequence having a modification which decreases or abrogates hydrogen bonding between same and a non-homopolymeric target sequence, thereby increasing the proportion of full length cDNA clones.

REMARKS

The new set of claims, which is now presented, is based on the original set thereof, amended in view of the Written Opinion and to better define the subject-matter of the present invention.

More specifically, claim 14 has been canceled since it was a duplicate of claim 13. Accordingly, claims 15-37 have been renumbered so as to become claims 14-36. Such language is amply supported by the disclosure, but specific support can be found, for example, at page 6, from lines 20 to 26. These amendments do not constitute new matter.

In view of the amendments to the claims and the arguments submitted above, it is respectfully submitted that the claims, which now more specifically relate to the destabilization between a modified homopolymeric region of an oligo and a non-homopolymeric sequence of a target nucleic acid, are novel and inventive.

In the unlikely event that the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **514012000100**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: April 8, 2002

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